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Cardiac troponin T: A sensitive and specific indicator of myocardial injury in patients with cerebrovascular stroke

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Abstract *Background:* Unsuspected morbidity and mortality in cerebrovascular stroke (CVS) patients remain a serious issue in critical medicine field. Patients with CVS are at increased risk of developing cardiac complications which explains the high morbidity and mortality rates among those patients. We examined the predictive value of cardiac troponin T (CTNT) in assessing myocardial injury and cardiac dysfunction in ischemic and hemorrhagic CVS.

Methods: One hundred and twenty patients with acute CVS (78 with infarction, 42 with hemorrhage) confirmed by brain CT scan were enrolled. CTNT assay was done within 24 h of stroke onset at 0, 12, and 24 h. Levels equal to or more than 0.1 ng/mL were deemed high. Echocardiographic evaluation was done at 3rd to 5th day for new segmental wall motion abnormalities (SWMA). Twelve lead electrocardiograms (ECGs) were done on day 1, 2, 3, and 5 from stroke onset. ST segment elevation or depression ≥ 1 mm, and/or T wave flattening or inversion in three leads were considered significant. Patients with history of CAD, resting ST-T wave changes were excluded.

Results: CTNT was elevated in 24 patients (20%), 12 patients with infarction (15.3%), and 12 with hemorrhage (28.5%), $P > 0.05$. Abnormal ECGs were observed in 50 cases (12 had ST deviation, 38 had T wave changes). All troponin +ve patients showed abnormal ECG (100%), compared to only 26 patients out of the troponin –ve patients (27%) ($P < 0.01$). ST deviation occurred in 10 troponin +ve patients (41.6%), two troponin –ve patients (2.08%), ($P < 0.01$). T wave changes occurred in 14 troponin +ve patients (58.3%), 24 troponin –ve patients (25%), ($P < 0.05$). Resting SWMA were observed in 24 cases, all of which had +ve troponin, none of the troponin –ve patients showed SWMA (100% sensitivity, specificity, positive and negative predictive values) $P < 0.001$.

Conclusions: Myocardial injury is not uncommon in patients with CVS. Silent ST-T wave changes and new resting SWMA are possible complications. We demonstrated highly significant correlation between positive troponin T and myocardial injury in these patients.

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1. Introduction

The need for multidisciplinary evaluation of patients with stroke has recently been established.¹ The role of cardiologist is highly relevant, given the multiple interactions between cardiovascular and cerebrovascular disease.² There are several reasons why the cardiologist should be closely involved in the management of patients with cerebrovascular stroke (CVS) or transient ischemic attacks (TIA).³ Ischemic stroke and TIA have a cardioembolic origin in 20–25% of cases⁴ and over 50% of patients with cerebrovascular disease may have coexisting coronary artery disease.⁵ Among stroke survivors, after the first year, the risk of death from non-stroke cardiovascular disease exceeds that of stroke.⁶

Unsuspected morbidity and mortality in cerebral stroke patients remain a serious issue in critical medicine field. Patients with cerebral stroke are at increased risk of developing cardiac complications which explains the high morbidity and mortality rates among stroke patients.⁷ Neurogenic influence on the heart is a newly well known phenomenon with pathological proof of myocytolysis and electrophysiological proof of cardiac conduction abnormalities.⁸

Biochemical markers are powerful and sensitive predictors of cardiac damage among cerebral stroke patients, so establishing correct prediction for high incidence of mortality and sudden deaths among stroke cases.⁹ Elevated activity of sympathetic nervous system and elevated systemic catecholamine levels induced by cerebral stroke are responsible for myocardial damage.¹⁰

We aimed at investigating the predictive value of cardiac troponin T (CTNT) in assessing myocardial injury and cardiac dysfunction in different types of stroke (ischemic and hemorrhagic) and its relationship to stroke size and volume.

2. Patients and methods

2.1. Study population

One hundred and twenty consecutive patients with acute stroke confirmed by CT scan of the brain, aged between 40 and 70 years, were included in this study which was conducted in the cardiology department of Police Authority Hospital in cooperation with neuropsychiatry department of the same hospital. Patients with the history of CAD, patients with resting ST-T wave changes (LBBB, WPW syndrome and patients on digitalis therapy), and patients with any condition that may elevate CTNT level (pulmonary embolism, congestive heart failure, cardiac trauma, renal impairment and myocarditis) were excluded from the study.

2.2. Methods

Careful history analysis including history of risk factors (e.g.: hypertension, smoking, diabetes mellitus, and dyslipidemia), general clinical assessment and physical examination with detailed cardiac and neurological evaluation was done for all patients.

2.2.1. Electrocardiography

Twelve lead ECG was done on 1st, 2nd, 3rd, 5th day after stroke. ST-T changes were considered significant if the patient

fulfilled at least one of the following criteria: more than 1 mm elevation or depression of ST segment and/or T wave inversion or flattening at least in three leads.¹¹

2.2.2. Echocardiography

Standard echocardiographic evaluation was performed on Vingmed CFM 800 system with a 2.5 MHz transducer on admission, then on the 3rd and 5th day. Standard views were used to assess resting segmental wall motion abnormalities (SWMA) as defined by the American society of echocardiography.¹² Myocardial dysfunction was diagnosed in the presence of new segmental wall motion abnormalities.¹³ All examinations were performed by one experienced echocardiographer who was blinded to CT results.

2.2.3. Biochemical markers

Troponin T assay was done within 24 h of stroke onset at 0, 12 and 24 h. Serum CTNT concentration was measured using the elecsys 2010 immunoassay system (Roche-Boehringer, Mannheim). Concentrations equal to or more than 0.1 ng/mL were deemed high.¹⁴ CPK, CK MB, LDH were also evaluated.

2.2.4. Brain CT scan

Using the CT images, the volume and the largest diameter of the cerebral lesions were calculated. Lesions were classified according to their largest diameter into: small lesions <1.5 cm, moderate lesions 1.5–3 cm, and large lesions >3 cm.¹⁵ Mild and moderate cases were combined in one group to ease further statistical comparisons.

An informed consent was given by all patients (or by close relative) and the study was approved by the local committee.

2.3. Statistical analysis

Data were collected, verified, revised, and edited on a personal computer; then statistically analyzed using SPSS statistical package version 12 and Microsoft excel 2003. The following tests were performed: mean and standard deviation, Chi square test (χ^2), ANOVA for analysis of variance, post Hoc test to detect least significant difference (LSD), and Student *t* test. *P* value <0.05 was considered, while *P* value <0.01 was considered highly significant.

3. Results

3.1. Demographic data and risk factors

This study included 120 patients: 70 (58.3%) males and 50 (41.7%) females, with a mean age of 60.25 ± 8.56 years. Hypertension was the most prevalent risk factor among the study group, followed by smoking, dyslipidemia, and diabetes mellitus, respectively (Table 1).

3.1.1. CT brain

Seventy-eight patients (65%) out of the population study presented with cerebral infarction, while 21 (25%) patients presented with cerebral hemorrhage (35%). Volume of the lesion ranged from 3 to 128 cm³ with a mean of 42.35 ± 30.18 cm³. Diameter of cerebral lesion ranged from 1 to 5 cm with a mean of 2.73 ± 0.82 cm. Twenty lesions (16.7%) were large lesions (>3 cm).

3.1.2. Biochemical markers

CKMB was elevated in 32 patients (26.7%) with a mean value of 25.88 ± 20.32 IU/L. Troponin T was elevated in 24 patients (20%) with a mean value of 0.14 ± 0.13 ng/mL.

3.1.3. Electrocardiographic and echocardiographic abnormalities

New ST-T wave changes were observed in 50 patients (41.6%): 38 (31.6%) patients showed T wave changes, while 12 (10%) patients showed ST deviation. Arrhythmias and conduction defects were observed in seven cases. Resting SWMA were observed in 24 cases (Table 2).

According to CTNT levels, patients were classified into troponin +ve patients ($n = 24$) and troponin -ve ($n = 96$) patients for further analysis.

3.2. Comparison between troponin +ve patients and troponin -ve patients

3.2.1. Regarding sex and risk factors

Hypertension and dyslipidemia were more prevalent in the troponin +ve group with no differences regarding gender or other risk factors (Table 3).

3.2.2. Regarding ECG

All troponin +ve patients showed abnormal ECG (100%), compared to only 26 patients out of the troponin -ve patients (27%), $P < 0.01$. ST deviation occurred in 10 troponin +ve

patients (41.6%) and 2 troponin -ve patients (2.08%), $P < 0.01$. T wave changes occurred in 14 troponin +ve patients (58.3%) and 24 troponin -ve patients (25%), $P < 0.05$ (Fig. 1).

3.2.3. Regarding echocardiography

Resting SWMA were observed in 24 cases, all of which had +ve troponin while none of the troponin -ve patients showed SWMA, $p < 0.0001$. According to the predefined criteria, troponin had 100% sensitivity, specificity, positive and negative predictive values for SWMA (Fig. 1).

3.2.4. Regarding cerebral lesion

Mean volume of the cerebral lesion was significantly higher in troponin +ve patients compared to that in troponin -ve patients. The diameter of the lesion was significantly larger in troponin +ve patients. Small to moderate lesions were observed in the majority of the troponin -ve patients (97.9%), while large lesions were present in most of the troponin +ve patients (75%) (Tables 4 and 5). No significant differences were noted in troponin +ve patients regarding the underlying pathology. CTNT was +ve in 12 patients with infarction and 12 patients with hemorrhage $p > 0.05$.

4. Discussion

Acute cerebrovascular insults may induce cardiac changes even in patients without coronary artery disease.¹⁶ Cardiac damage in acute stroke has been studied by measuring creatine kinase myocardial band (CK-MB) or by autopsy. These studies lacked neuroimaging confirmation of stroke. Neurological injury can produce ECG changes, cardiac dysfunction, and focal cardiac injury.¹⁷ Such changes are well characterized after subarachnoid hemorrhage and head trauma.¹⁶ Previous studies¹⁷⁻²⁰ of serum markers of myocardial injury in acute stroke did not include neuroimaging confirmation of stroke, or CTNT determination, unlike the present study. Myocardial injury after stroke or other acute cerebral lesions was attributed to abnormally high levels of plasma catecholamine secondary to rapidly increasing intracranial pressure.²¹ Currently cardiac troponins are considered the most accurate biomarker of myocardial injury in the clinical setting.

In the current study, 120 patients with acute CVS were studied using the troponin T assay. One fifth of the stroke patients had elevated CTNT. James et al.⁷ reported elevated CTNT in about 17% of their samples, while Julio A. Chalela et al.¹⁸ reported elevated CTNT in 6%.

Table 1 Risk factors among the study group.

	No.	%
Hypertension	60	50
Current smokers	58	48.3
Dyslipidemia	52	43.3
Diabetes	28	23.3

Table 2 ECG changes and echocardiographic data among the study group.

	No.	%
ST deviation	12	10
T	38	31.6
AF	6	5
RBBB	1	0.83
SWMA	24	20

Table 3 Comparison between troponin +ve patients and troponin -ve patients regarding sex and risk factors.

		Troponin +ve (24)		Troponin -ve (96)		P
		No.	%	No.	%	
Gender	M	14	58.33	56	58.33	NS
	F	10	41.67	40	41.67	
Diabetes		8	33.33	20	20.93	NS
Smoker		12	50	46	47.92	NS
Dyslipidemia		18	75	34	35.42	<0.05
Hypertension		24	100	36	37.5	<0.01

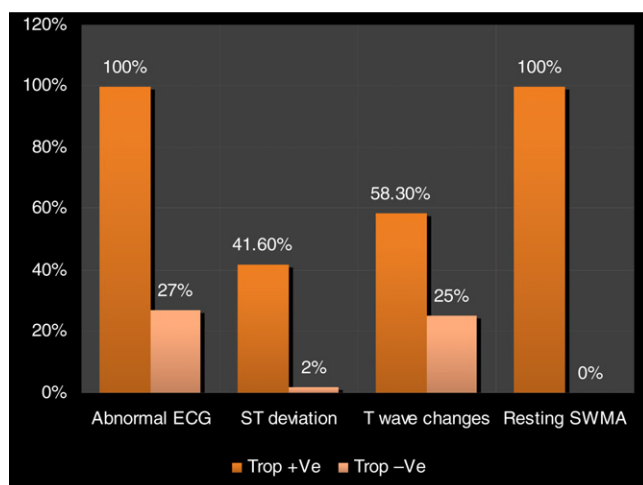


Figure 1 ST-T wave abnormalities and SWMA in troponin +ve and troponin -ve patients.

The current study showed significant prevalence of hypertension and dyslipidemia in stroke patients with elevated troponin levels versus stroke patients with normal troponin levels. This may give a good explanation to the occurrence of myocardial injury in these possibly due to the presence of more vulnerable coronary plaques. We also suggest that some risk factors may carry the power to prepare myocardial vasculature to the harmful effect of the released catecholamines (stress myocardial injury).

4.1. ECG findings among stroke patients with elevated troponin levels versus patients with normal levels

Earlier studies reported contradictory findings about the ST-T changes observed in acute stroke patients.²² They detected ST changes in 26.31% of patients and T changes in 28%. Others reported ST changes in 39–50% and T wave changes in 25–50% of patients.¹⁹ In this study, we demonstrated significant differences regarding ST-T wave, between stroke patients with elevated troponin levels versus stroke patients with normal troponin levels. Although the majority of the previous studies stated that the ST-T changes in these patients are non specific,²³

the correlation between elevated CTNT levels and echocardiographic abnormalities in this study and other studies may give us a clue that these ST-T abnormalities were due to myocardial ischemia or/and injury.²⁴

4.2. Echocardiographic results among stroke patients with elevated troponin levels versus patients with normal levels

The current study showed a significant difference in wall motion abnormalities between stroke patients with elevated troponin levels versus stroke patients with normal levels. All (100%) patients with elevated troponin levels had segmental wall motion abnormalities. Several studies reported a significant correlation between echocardiographic changes and CTNT levels.^{25–27} Moreover, a significant inverse correlation was reported between elevated CTNT levels and LV ejection fraction.²⁷

4.3. Stroke volume and its relation to elevated CTNT levels

This study showed a significant positive correlation between elevated CTNT levels and increased volume of the cerebral lesion as demonstrated via CT scan. Similar findings were reported by Apak et al.²⁶ and Panteghini et al.²⁷ This may be explained by the amount of catecholamine release (surge), which is possibly directly correlated to the size of the cerebral lesion.

5. Conclusions

Myocardial injury is not uncommon in patients with CVS. Myocardial injury was demonstrated in one fifth of the patients of this study. Silent ST-T wave changes and new resting SWMA are possible complications. CTNT is a sensitive marker in detecting myocardial injury after cerebral stroke that also correlates with the size of the cerebral lesion. Measurement of the serum level of CTNT may provide a useful aid in estimating the volume of stroke lesion and possibly the prognosis of the stroke in clinical practice. Future therapies may be directed toward preventing cardiac events in CVS patients, thereby reducing overall morbidity and mortality.

Table 4 Comparison between troponin +ve patients and troponin -ve patients regarding volume and diameter of the cerebral lesion.

	Troponin T +ve (24)	Troponin T -ve (96)	<i>T</i>	<i>P</i>
	Mean ± SD	Mean ± SD		
Volume (cm ³)	96.92 ± 16.3	28.71 ± 11.45	16.88	<0.001
Diameter (cm)	3.83 ± 0.58	2.46 ± 0.62	6.98	<0.001

Table 5 Comparison between troponin +ve patients and troponin -ve patients regarding severity of cerebral lesion.

	Troponin T +ve (24)		Troponin T -ve (96)		χ^2	<i>P</i>
	No.	%	No.	%		
Small	6	25	94	97.92	36.75	<0.001
Large	18	75	2	2.08		

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